CASE REPORT

Symptomatic *Blastocystis* spp. infection among returners from intertropical regions – is the diagnostics of acquired immunodeficiency necessary?

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Abstract

Blastocystis hominis (stramenopila), an absolute anaerobic organism, has been considered a commensal of human large intestine, as even its massive invasion usually is asymptomatic. Nowadays, *Blastocystis* spp. has been mentioned more frequently as a potential etiologic agent of a chronic diarrhea, mainly among immunocompromised individuals, but also among patients with functional bowel disorders, malnourished, with chronic disease, or after organs transplantations. *Blastocystis* may also be responsible for traveler's diarrhea.

Gastrointestinal disorders are quite common problems for individuals returning from different climatic and sanitary areas – countries located mainly in the tropics. Majority of such cases are patients suffering from self-limiting gastrointestinal tract. However, some patients, especially those who do not respond to empirical treatment in the primary health care, require more specialized diagnostics; this applies to the group of patients with prolonged diarrhea. Usually, they are caused by *Escherichia coli* infection. In this paper, we describe two travelers from Africa and India with prolonged diarrhea. The parasitic stool evaluation revealed massive *Blastocystis hominis* infestation. It was the reason to provide further diagnostics for acquired immunodeficiency, which gave the final diagnosis of HIV infection.

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Key words: *Blastocystis* spp., diarrhea, diagnostics, HIV.

Introduction

Gastrointestinal disorders are quite common problems for individuals returning from different climatic and sanitary areas – mainly countries located in the intertropical regions. In majority of such cases, patients suffer from self-limiting disorders. However, some patients, especially those who do not respond to empirical treatment in the primary health care, require more specialized diagnostics for gastrointestinal infections; this applies to the group of patients with prolonged diarrhea. They suffer from numerous watery, sometimes bloody loose stools as well as abdominal cramps, flatulence, nausea, vomiting, and loos of appetite. The most common disorder diagnosed after returning from tropics is the traveler's diarrhea [1] and *Escherichia coli* (EHEC) [2], which is the most frequently diagnosed etiological agent. Other factors responsible for the traveler's diarrhea include protozoa such as *Giardia intestinalis*, *Entamoeba histolytica*, as well as coccidian parasites from Api-complex family, such as *Cryptosporidium* spp., *Cystoisospora* spp., *Cyclospora* spp. [3], and

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very frequently reported *Blastocystis hominis* [4]. During international journeys, especially touristic holidays, people often forgot to comply with the rules of tropical hygiene that poses a threat for parasitic infections of small and large intestine. It should be emphasized that patients with intestinal protozoan can be a potential source of epidemiological risk to their environment, because even asymptomatic patients defecate parasite cysts, which are potentially contagious for other people. Immunocompromised patients are especially vulnerable to GI tract infections, which are typically asymptomatic and self-limiting among immunocompetent patients. Chronic, wasting diarrhea in the course of intestinal cryptosporidiosis, is typical for HIV-infected patients, which is one of the acquired immune deficiency syndrome (AIDS) indicators [5, 6]. In both developed and developing countries, parasitic infections continue to be a frequent cause of gastrointestinal disorders. GI protozoa are progressively becoming recognized as important pathogens in patients that are immunocompromised [7].

Case reports

In this article, the cases of two patients will be discussed. The first patient is a 41-years-old white male, who was urgently admitted to the Clinic of Tropical and Parasitic Diseases due to fever, papular rash, and diarrhea (up to 8 loose stools per day), in which dengue fever was suspected. The patient started to feel uncomfortable after coming back to Poland from Republic of South Africa, where he had worked for 3 years. During his stay in Africa, this patient didn't use any chemoprophylaxis against malaria. On admission, patient was febrile. Dorsal, thoracic exanthema as well as a low lip herpes were identified. In addition, reddened mucous of the throat and white lesions on tongue were also found. While performing peripheral blood investigation (thick drop and thin smear), different *Plasmodium* spp. forms were not found.

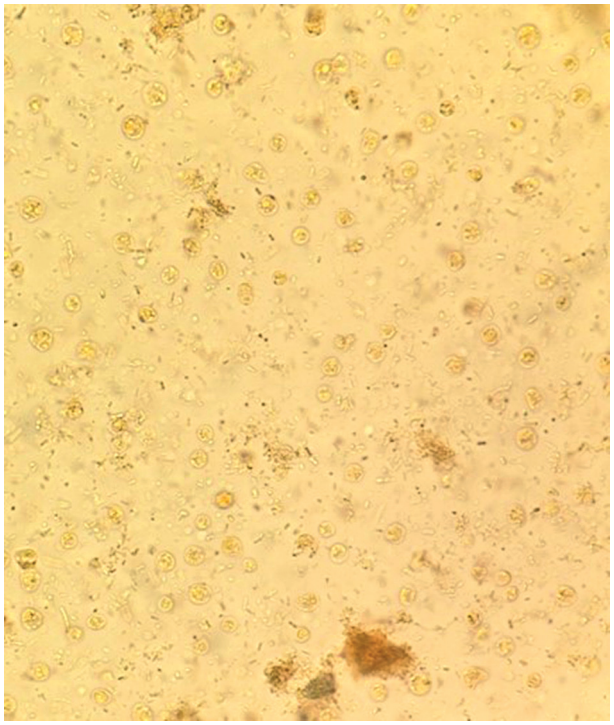

Figure 1. Numerous cystic and amoebic forms of *Blastocystis hominis*

Leukopenia and thrombocytopenia had been reported in laboratory studies. These findings together with skin rash, have raised suspicion of dengue hemorrhagic fever, which was excluded by serological testing using immunoassays ELISA, which detects IgM and IgG. In addition, antibodies against dengue and immunoblot test for kala-azar disease (visceral leishmaniosis) were also performed with negative results. Stool microscopic investigations revealed many cystic, amoeboid, granular forms of *Blastocystis* spp. (iodine staining). Furthermore, cysts of *Entamoeba histolytica/dispar* were detected, and a test for the presence of blood in the stool was positive. Moreover, *Candida albicans* and methicillin sensitive strain of *Staphylococcus aureus* were grown in the swab from the throat. Gastroscopy revealed gastroduodenitis and urease test confirmed *Helicobacter pylori* infection. Specific therapy of *Blastocystis/Entamoeba* gastrointestinal co-infection was initiated, using co-administration of paromomycin, metronidazole, and fluconazole. After two weeks' treatment, the full eradication of protozoa was achieved. The massive infection of *Blastocystis* spp. (Figure 1) with severe clinical symptoms contributed to the diagnosis of acquired immunodeficiency syndrome.

The IV generation test for HIV infection (detecting HIV-1, HIV-2 antibody and p24 antigen) was performed twice with very high, positive results (1,054; 78 S/CO). CD4 cell count 390/µl. Western blot was negative. HIV quantitative RNA test (RT-PCR using primers and probes specific for HIV-1 genome fragment) was used, and no genetic material of the virus was detected. During the detailed interview, the patient admitted having risky heterosexual behaviors with the natives. Western-Blot negative results and RT-PCR inhibitory response might had been associated with HIV-2 infection, which characterizes with a very low replication rate in most cases [8] (African strain?) or very early infection period [9]. At the same time, the diagnostics of viral hepatitis (HBsAg, anty-HCV) and syphilis (RPR, TPHA) were performed. All those tests were negative. However, serological exponents of late *Toxoplasma gondii* infection were demonstrated (ELISA IgG). After the treatment of parasitic invasion, suspecting HIV infection, the patient was transferred for further diagnostics to the Department and Clinic of Infectious Diseases (Poznan, Poland), where retesting (immunoblot-reaction with the polypeptides p17, p31, gp41 p24, sgp120 characteristic for HIV-1 infection were found, RT-PCR HIV-RNA) finally confirmed the diagnosis of HIV infection.

The second patient, 49-year-old white male, was transferred to the Department of Tropical and Parasitic Diseases from the Gastroenterology Clinic due to symptomatic infec-

tion of *Blastocystis* spp. Parasitic stool examination revealed single protozoan forms of this parasite (iodine staining). This patient was admitted to the Gastroenterology Clinic due to chronic diarrhea (up to 10-12 loose stools per day), without blood and mucus, and weight loss of about 10 kg within 5 months, with suspected microscopic enteritis. Preliminary diagnosis was performed on the basis of histopathological examination of samples taken during outpatient colonoscopy. The patient's complaints appeared about 5 months earlier, just after 3-week holidays in Thailand. Ambulatory oral treatment with budesonide and mesalazine had not given any clinical effects. At the time of admission to the Department of Tropical and Parasitic Diseases, the patient was emaciated. Pallor, enlarged, hard, and painless cervical lymphnodes were found. Basic laboratory investigations revealed hypokalemia, hypoalbuminemia, hypoproteinemia, mild hypertransaminasemia. *Clostridium difficile* glutamate dehydrogenase test was positive. *C. difficile* infection was finally excluded, using the assay for the gene of *C. difficile* toxins. There were no significant deviations in ultrasound of the abdominal cavity. Computed tomography of the abdomen revealed thickened wall of the large intestine, with single gas/fluid levels. Gastroscopy revealed endoscopic changes characteristic for esophageal mycosis. Presence of *Candida albicans, Sphingomonas paucimobilis*, and *Staphylococcus aureus* were detected. Due to a vague clinical picture and no response to typical treatment of inflammatory bowel disease, test for HIV infection was performed twice; the results have been positive (IV generation HIV1-2 antibody assay/p24 antigen test). The positive result of the screening test was confirmed by the Western-Blot test (in the assay reaction with polypeptides p17, p24, p31, gp41, sgp120, characteristic for HIV-1 infection, were found). Estimated number of CD4 in flow cytometry was 58/μl. HIV-RNA (RT-PCR test) was 5,260 copies/μl. Quantiferon TB-Gold test had a negative result. Metronidazole causative treatment, potassium supplementation, fluconazole, and trimethoprim with sulfamethoxazole (as a primary prophylaxis of pneumocystis pneumonia) have been introduced. The 14-day-treatment improved the clinical status of the patient, and the number of loose stools decreased. After, 3-week hospitalization, the patient was discharged home with a recommendation for further treatment in the Acquired Immunodeficiency Outpatient Department.

Discussion

Blactocystis hominis (stramenopila), an absolute anaerobic organism, has been considered a commensal of human large intestine [10, 11], as even its massive invasion usually is asymptomatic. Nowadays, *Blastocystis* spp. has been mentioned more frequently as a potential etiologic agent of a chronic diarrhea, mainly among immunocompromised individuals, but also among patients with functional bowel disorders, malnourished, with chronic disease such as oncological patients, and after organs transplantation [12-15]. Moreover, this parasite has a significant role in enhancing carcinogenesis by resulting damage to the intestinal epithelium [16]. *Blastocystis* may also be responsible for the traveler's diarrhea [3, 17]. It is one of the most commonly detected fecal parasite among people returning from developing countries, which are common destinations for tourists. *Blastocystis* infection rates are higher than 20% [18]. *Blastocystis hominis* is a unique organism that occurs in many morphological forms (vacuolar, amoebic, cystic). Infection occurs when invasive forms of this parasite are ingested with contaminated water, unwashed fruits or vegetables [19]. *Blastocystis*, similarly to *Entamoeba histolytica*, probably might be also transmitted between people during sexual anal contacts (such statement requires more investigations). Infection, if symptomatic, leads to watery diarrhea, sometimes with blood, which can quickly cause significant dehydration with secondary consequences for the host organism.

Chronic diarrhea, for which no etiologic agent has been established, should prompt physicians to undergo detailed parasitological investigation for atypical intestinal protozoa such *Blastocystis hominis*. Diagnostics for HIV infection should be considered when different morphological forms of this organism are detected in the stool samples and when patient is symptomatic. Patients with HIV infection are more prone to gastrointestinal infections causing diarrhea, particularly with parasites. Parasitic infections, GI protozoa mainly have been regularly reported in such patients. More frequently, presence of *Blastocystis* spp. forms in stool examinations among HIV-infected patients has been demonstrated [20, 21]. Symptomatic *Blastocystis* such as cryptosporidiosis may be recognized as opportunistic infection among HIV-infected individuals [22]. Although simple and cheap, parasitological microscopic investigation of stool sample is a very important method of recognizing invasions of gastrointestinal tract. Therefore, it has lower sensitivity and higher specification than genetic diagnostic methods (PCR) [23]. Usage of different staining is essential for detection of developmental forms of different parasites (e.g., acid-fast staining when coccidial infection is suspected (*Cyclospora* spp., *Cryptosporidium* spp.) [24]. It should be highlighted that this diagnostic method requires an experienced person to evaluate the sample. HIV infection directly impairs proper function of the gut-associated lymphoid tissue (GALT). HIV enteropathy may lead to diarrhea directly through structural and immunological damage of the intestine mucosa [25]. Parasitic invasions caused by intestinal protozoa such as *Blastocystis* spp., *Cyclospora* spp., and *Clostridium* spp., contribute to a greater destruction of intestinal villi, resulting in significant increase of gastrointestinal symptoms. Low level of immunologic response contribute to secondary infections of the gastrointestinal tract caused by both opportunistic and non-opportunistic parasitic inoculation [26].

Conclusions

Microscopic examination of stool specimen should be one of the basic, routinely performed tests in case of chronic diarrhea, especially among individuals who are suspected or confirmed to suffer from human immunodeficiency

virus infection. Early and proper detection of enteric parasitic infections will help in the management and can improve the quality of life for HIV-infected individuals [27].

Conflict of interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

1. Pitzurra R, Steffen R, Tschopp A, Mutsch M. Diarrhoea in a large prospective cohort of European travellers to resource-limited destinations. BMC Infect Dis 2010; 10: 231.
2. Shah N, DuPont HL, Ramsey DJ. Global etiology of travelers' diarrhea: systematic review from 1973 to the present. Am J Trop Med Hyg 2009; 80: 609-614.
3. Kłudkowska M, Pielok Ł, Frąckowiak K, Paul M. Intestinal coccidian parasites as an underestimated cause of travellers' diarrhoea in Polish immunocompetent patients. Acta Parasitol 2017; 62: 630-638.
4. Herbinger KH, Alberer M, Berens-Riha N, et al. Spectrum of Imported Infectious Diseases: A Comparative Prevalence Study of 16,817 German Travelers and 977 Immigrants from the Tropics and Subtropics. Am J Trop Med Hyg 2016; 94: 757-766.
5. Huppmann AR, Orenstein JM. Opportunistic disorders of the gastrointestinal tract in the age of highly active antiretroviral therapy. Hum Pathol 2010; 41: 1777-1787.
6. Lepczyńska M, Białkowska J, Dzika E, Piskorz-Ogórek K, Korycińska J. Blastocystis: how do specific diets and human gut microbiota affect its development and pathogenicity? Eur J Clin Microbiol Infect Dis 2017; 36: 1531-1540.
7. Siddiqui ZA. An overview of parasitic infections of the gastrointestinal tract in developed countries affecting immunocompromised individuals. J Parasit Dis 2017; 41: 621-626.
8. Bertine M, Gueudin M, Mélard A, et al. New Highly Sensitive Real-Time PCR Assay for HIV-2 Group A and Group B DNA Quantification. J Clin Microbiol 2017; 55: 2850-2857.
9. Alexander TS. Human Immunodeficiency Virus Diagnostic Testing: 30 Years of Evolution. Clin Vaccine Immunol 2016; 23: 249-253.
10. Shah N, DuPont HL, Ramsey DJ. Global etiology of travelers' diarrhea: systematic review from 1973 to the present. Am J Trop Med Hyg 2009; 80: 609-614.
11. Roberts T, Stark D, Harkness J, Ellis J. Update on the pathogenic potential and treatment options for Blastocystis sp. Gut Pathog 2014; 6: 17.
12. Siddiqui ZA. An overview of parasitic infections of the gastro-intestinal tract in developed countries affecting immunocompromised individuals. J Parasit Dis 2017; 41: 621-626.
13. Salvador F, Sulleiro E, Sánchez-Montalvá A, et al. Epidemiological and clinical profile of adult patients with Blastocystis sp. infection in Barcelona, Spain. Parasit Vectors 2016; 9: 548.
14. Rasti S, Hassanzadeh M, Hooshyar H, et al. Intestinal parasitic infections in different groups of immunocompromised patients in Kashan and Qom cities, central Iran. Scand J Gastroenterol 2017; 52: 738-741.
15. Mohamed AM, Ahmed MA, Ahmed SA, et al. Predominance and association risk of Blastocystis hominis subtype I in colorectal cancer: a case control study. Infect Agent Cancer 2017; 12: 21.
16. Kumarasamy V, Kuppusamy UR, Jayalakshmi P, et al. Exacerbation of colon carcinogenesis by Blastocystis sp. PLoS One 2017; 12: e0183097.
17. van Hattem JM, Arcilla MS, Grobusch MP, et al. Travel-related acquisition of diarrhoeagenic bacteria, enteral viruses and parasites in a prospective cohort of 98 Dutch travelers. Travel Med Infect Dis 2017; 19: 33-36.
18. del Coco VF, Molina NB, Basualdo JA, Córdoba MA. Blastocystis spp.: avances, controversias y desafíos futuros. Rev Argent Microbiol 2017; 49: 110-118.
19. Thompson RC, Smith A. Zoonotic enteric protozoa. Vet Parasitol 2011; 182: 70-78.
20. Albrecht H, Stellbrink HJ, Koperski K, Greten H. Blastocystis hominis in human immunodeficiency virus-related diarrhea. Scand J Gastroenterol 1995; 30: 909-914.
21. Deepika K, Rajkumari N, Liji AS, et al. Multiple parasitic and viral infections in a patient living with HIV/AIDS on antiretroviral therapy. Indian J Med Microbiol 2017; 35: 432-435.
22. Gassama A, Sow PS, Fall F, et al. Ordinary and opportunistic enteropathogens associated with diarrhea in Senegalese adults in relation to human immunodeficiency virus serostatus. Int J Infect Dis 2001; 5: 192-198.
23. Saigal K, Khurana S, Sharma A, et al. Comparison of staining techniques and multiplex nested PCR for diagnosis of intestinal microsporidiosis. Diagn Microbiol Infect Dis 2013; 77: 248-249.
24. Mauss J, Retz M, Dilts R, Langland J. Multiple Sampling and SAF-Fixative Triple-Faeces Testing for Dysbiosis and Pathogenic Infections of the Gastrointestinal Tract: Case Report. Altern Ther Health Med 2017; pii: AT5587.
25. Brenchley JM, Douek DC. The mucosal barrier and immune activation in HIV pathogenesis. Curr Opin HIV AIDS 2008; 3: 356-361.
26. Ghimire A, Bhandari S, Tandukar S, et al. Enteric parasitic infection among HIV-infected patients visiting Tribhuvan University Teaching Hospital, Nepal. BMC Res Notes 2016; 9: 204.
27. Sherchan JB, Ohara H, Sakurada S, et al. Enteric opportunistic parasitic infections among HIV seropositive patients in Kathmandu, Nepal. Kathmandu Univ Med J (KUMJ) 2012; 10: 14-17.